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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,252	06/09/2005	Dirk A Heerding	P51399	1871

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EXAMINER	
HAVLIN, ROBERT H	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
07/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,252	HEERDING ET AL.	
	Examiner	Art Unit	
	Robert Havlin	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-55* is/are pending in the application.

4a) Of the above claim(s) *55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims: Claims 45-55 are currently pending. On 5/1/07 applicant cancelled claims 1-44 and provided new claims 45-55.

Priority: This application is a 371 of PCT/US03/39633 (12/12/2003) which claims benefit of 60/433,482 (12/13/2002).

IDS: The IDS of 6/9/2005 and 11/22/2006 have been considered.

Election/Restrictions

1. Applicant's election without traverse of the combined group VI and VII in the reply filed on 5/1/2007 is acknowledged.

In a telephone interview on 7/2/2007 applicant agreed to elect the method of using products in the invention. Based on applicant's arguments, the examiner has agreed to rejoin the method of use groups VI and VII for examination which encompass the amended claims 45-54. Claim 55 which is drawn to a product is hereby withdrawn from consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

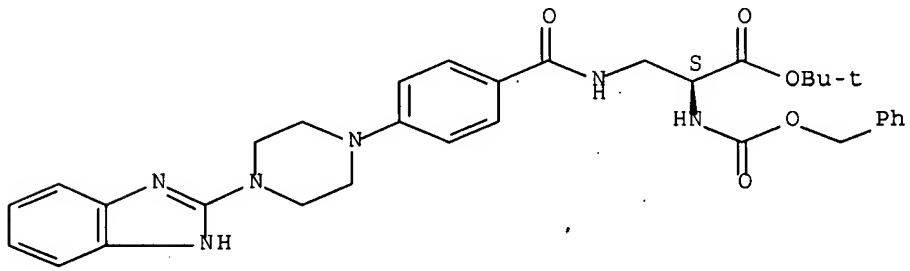
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 45-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Ajito et al.** (WO 99/38849, US 6451800), in view of **Ayal-hershkovitz et al.** (WO 02/060374) and **Raeymaekers et al.** (US 4,859,684).

The claimed subject matter in claims 45-54 read on methods of treating thrombocytopenia in mammals and humans by providing a therapeutic agent including a benzimidazole compound. Furthermore, the application also claims a method of agonizing a TPO (thrombopoeitin) receptor with the same compound.

Determination of the scope and content of the prior art

Ajito et al. teaches treating humans for thrombocytopenic conditions with a genus of compounds including benzimidazoles such as



The compounds are taught to have activity by acting on a receptor. Furthermore, the specification describes the utility of the compounds taught as:

> (95) Use of compounds/pharmaceutical composition
>
> (96) The compounds according to the present invention have potent integrin .alpha..sub.v.beta..sub.3 antagonistic activity, as demonstrated in Pharmacological Test Example 1. The integrin .alpha..sub.v.beta.3 mediates cardiovascular diseases such as acute myocardial infarction, neointima formation hypertrophy, restenosis after PTCA/stent operation, unstable angina, acute coronary syndrome, angina pectoris after PTCA/stent operation, or arterial sclerosis, particularly atherosclerosis; angiogenesis-related diseases such as diabetic retinopathy, diabetic vascular complication, or vascular grafting; cerebrovascular diseases such as cerebral infarction; cancers such as solid tumors or metastasis thereof; immunological diseases such as arthritis, particularly rheumatic arthritis; and osteopathy such as osteoporosis, hypercalcemia, periodontitis, hyperparathyroidism,

periarticular sore, or Paget's diseases (DN & P, 10 (8), 456 (1997)). Accordingly, the compounds according to the present invention can be used in the treatment of these diseases. The term "therapy" or "treatment" as used herein includes "prevention" or "prophylaxis."

(97) As described in Pharmacological Test Example 2, **the compounds according to the present invention have GP IIb/IIIa antagonistic activity** and human platelet aggregation inhibitory activity. Therefore, **the compounds according to the present invention can be used in the treatment of platelet thrombosis and thromboembolism** during and after the treatment of thrombolysis and after angioplasty of the coronary artery and other arteries and after bypassing of the coronary artery, the improvement of peripheral circulating blood stream, and the inhibition of blood clotting during extracorporeal circulation. **Furthermore, the compounds according to the present invention can be used in the treatment of thrombotic thrombocytopenic purpura** and hemolytic uremic syndrome (Gendai Iryo, 29, (11), 2753 (1997)).

And in the claims:

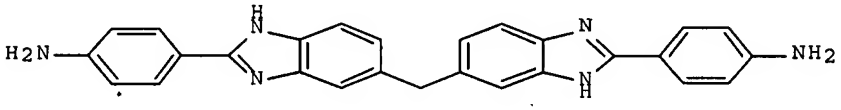
11. A method for treating platelet thrombosis or thromboembolism, the improvement of peripheral circulating blood stream, the inhibition of blood clotting during extracorporeal circulation, or the treatment of thrombotic thrombocytopenic purpura or hemolytic uremic syndrome, comprising the step of administering an effective amount of a compound represented by formula (I) or a pharmaceutically acceptable salt or solvate thereof: ##STR199## ...

22. A method for treating platelet thrombosis or thromboembolism, the improvement of peripheral circulating blood stream, the inhibition of blood clotting during extracorporeal circulation, or the treatment of thrombotic thrombocytopenic purpura or hemolytic uremic syndrome, comprising the step of administering an effective amount of a compound of claim 20 or a pharmaceutically acceptable salt or solvate thereof together with a pharmaceutically acceptable carrier, to mammals including humans.

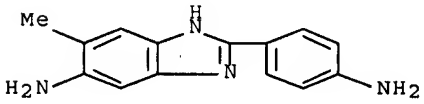
23. A method for inhibiting platelet aggregation, comprising the step of administering an effective amount of a compound of claim 20 or a pharmaceutically acceptable salt or solvate thereof together with a pharmaceutically acceptable carrier, to mammals including humans.

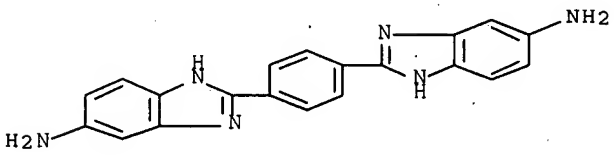
24. The method according to claim 19 wherein the .alpha..sub.v.beta..sub.3 mediated disease is atherosclerosis or rheumatic arthritis.

Ayal-hershkovitz et al. (WO 02/060374) teaches the use of a genus of benzimidazole compounds, such as those below, for the treatment of thrombocytopenia in a preferred embodiment on page 28, paragraph 3.

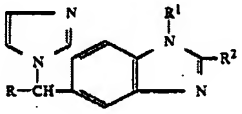


I





Raeymaekers et al. (US 4,859,684) teaches the numerous compounds falling into the genus of formula I including the table from page 38:



No. R	R^1	R^2	salt/base	mp (°C.)
40 H	H	(3-pyridinylmethyl)	3 HCl	254.5
41 H	H	2-CH_3O—C_6H_4	base	185.3
42 H	H	3-CH_3O—C_6H_4	base	169.7
43 H	H	(2-pyridinylmethyl)	3 HCl.½ H_2O	222.2
44 H	H	n-C_6H_{13}	2 $(COOH)_2$.½ H_2O	101.8
45 H	H	(4-pyridinyl)CH=CH	base,E-form	234.1
46 H	H	(3-pyridinyl)CH=CH	3 HCl.H_2O	270.3
47 H	H	2-thienyl	base	196.4
48 H	H	(1H—imidazol-5-yl)-CH=CH	3 HCl.1½ H_2O	237.0
49 C_6H_5	H	4-CH_3O—C_6H_4	base	236.5
50 H	H	2-CH_3—C_6H_4	2 $(COOH)_2$	176.0
51 H	H	4-thiazolyl	2 HCl.2 H_2O	147.6
52 H	H	3-quinolinyl	base	> 300
53 H	H	2-NH_2—3-pyridinyl	base	267.5
54 C_2H_5	H	C_6H_5	base	203.7
55 C_2H_5	H	4-F—C_6H_4	base	197.4
56 i-C_4H_9	H	4-F—C_6H_4	base	187.9
57 n-C_4H_9	H	C_6H_5	base	153.4
58 CH_3	H	4-F—C_6H_4	base	191.1
59 i-C_4H_9	H	C_6H_5	1½ $(COOH)_2$.½ H_2O	105.5
60 CH_3	H	C_6H_5	base	196.2
61 n-C_4H_9	H	4-F—C_6H_4	base	163.8
62 CH_3	CH_3	C_6H_5	2 $(COOH)_2$	144.6
63 CH_3	CH_3	4-F—C_6H_4	2 $(COOH)_2$	151.0

Differences between the prior art and the claims

Ajito et al. does not teach the identical genus or species of compounds as in the instant invention, however it does teach the same method of use for related compounds. Ayal-hershkovitz et al. teaches compounds closely related to the instant invention for use in treating thrombocytopenia but does not teach the identical species. Raeymaekers et al. teaches the compounds of the instant invention, but for a different method of use.

Finding of prima facie obviousness – rationale and motivation

The teachings of Ajito et al. and Ayal-hershkovitz et al. for the treatment of thrombocytopenia in humans using a genus of benzimidazole compounds reasonably suggests to one of ordinary skill in the art to use benzimidazole compounds taught therein as well as those taught by Raeymaekers et al. due to the compounds belonging to the same art recognized class. Therefore, it would have been obvious to one of ordinary skill in the art to use benzimidazole compounds for the treatment of thrombocytopenia in humans. Furthermore, the method of agonizing a TPO receptor would have been obvious to one of skill in the art since the method is using the compound in the manner in which it was taught by the prior art.

Conclusion

All claims are rejected.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Havlin whose telephone number is (571) 272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert Havlin
Examiner

RH

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER